A kinetic-based protocol for acute hyperammonaemia in neonates using CarpeDiem and Fresenius 4008 machine

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Introduction and management question

Acute hyperammonaemia in children is associated with poor neurological outcomes and high mortality. As theses outcomes are inversely correlated to the duration of the hyperammonaemic coma, prompt management with conservative treatment with/without renal replacement therapy is needed. Cardio-Renal Pediatric Dialysis Emergency CRRT Machine (CarpeDiem) is demonstrated a safe and effective CRRT machine in neonates and infants. Experience on its use in acute hyperammonaemia is limited.

As neurological outcomes are related to the duration of the hyperammonaemic coma, management should aim to decrease serum ammonia levels below 400 µmol/L in a short period of time (ideally less than 4 hours). Therefore, we formulated the following management question in our unit: *"How efficient can CARPEDIEM CRRT machine decrease serum ammonia levels in comparison to 4008 Fresenius machine? How can we safely incorporate CARPEDIEM in our local protocol using a kinetic-based approach, ensuring a decrease in serum ammonia below 400 µmol/L in less than 4 hours ?"*

Methods

To answer this management question, we reviewed four patients who were treated with hemodialysis between 2019-2020 with different dialysis machines, i.e. either hemodialysis (HD) with the 4008 machine and FX Paed dialyzer (Fresenius Medical Care, Bad Homburg, Germany), and/or continuous veno-venous hemodialysis (CVVHD) with the CarpeDiem machine and the 0.15m² or the 0.25m² dialyzer (Medtronic, Minnesota, USA).

Dialyzer clearance, and with it, dialyzer extraction ratio was derived from the ammonia concentration-time curves during dialysis, in the four tested patients. Ammonia was hereby assumed being distributed in a single compartment in the patient of 60% of total body weight. Serum ammonia level was thus expected to follow an exponential decline during dialysis. Generation was derived from the concentration increase in the interdialytic interval, assuming the patients to be in a rather steady state during the time period of calculation. Single compartmental models for an average child of 2, 3, 4 and 5kg were further used to simulate ammonia concentration for different ammonia start concentrations (i.e. 3000, 1500, 800, 400, and 200µmol/L), dialysis machines/dialyzers and different dialysis settings (i.e. blood flow Q_B of 30-50mL/min).

Results

The four patients (3.24±0.40 kg) underwent 13 dialyses, i.e. 5 with the 4008-FXPaed, and 8 with the CarpeDiem of which 4 with the 0.15m² and 4 with the 0.25m² dialyzer. Blood flows were 30-35mL/min (4008-FXPaed), 22-35mL/min (Carpe Diem 0.15), and 30-34mL/min (Carpe Diem 0.25).

Extraction ratios were 38±5% in the FXPaed on the 4008 dialysis machine, 10±3% and 13±3% in the 0.15m² and 0.25m² dialyzer, respectively on the CarpeDiem. Generation was 0.40±0.25µmol/min, having no impact on the calculation of dialyzer clearance and extraction ratio.

For a start concentration of 3000µmol/L in a patient of 3kg, the time to reach the target of 400µmol/L was, with the 4008-FXPaed, 315 and 190min for a Q_B of 30 and 50mL/min, respectively, while it was 205 and 125min for a start concentration of 1500µmol/L, and 110 and 65min for a start concentration of 800µmol/L. The CarpeDiem machine was found inadequate to decrease ammonia concentrations within 4h for start concentrations higher than 800µmol/L. Simulations in a patient of 5kg resulted in longer time intervals to reach the target for the 4008-FXPaed, while targets cannot be reached within 4h with the CarpeDiem.

Based on the results of these simulations, a local protocol for acute hyperammonaemia was developed aiming to reach serum ammonia levels below 400µmol/L within 4 hours after diagnosis, and a serum ammonia level below 200µmol/L within the following 4 hours. Taking into account these management goals, Carpe Diem was incorporated in our local protocol as first line renal replacement therapy in neonates presenting with a hyperammonaemic coma and serum ammonia levels between 200-400µmol/L. In neonates presenting with ammonia levels higher than 400µmol/L, Fresenius 4008 machine (Q_B 50mL/min) was used as first line treatment until serum ammonia levels dropped below 200µmol/L. At this point Fresenius 4008 was switched to CarpeDiem to avoid rebound of serum ammonia levels.

Conclusion

Kinetic models can guide our management decisions and treatment protocols by predicting which treatment goals can be reached with a particular dialysis prescription, available resources and/or dialysis modality.